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13. ABSTRACT (Maximum 200 words) <p>The basic goal of our research program is to localize and analyze processes and mechanisms of memory formation, storage and retrieval in the mammalian brain. We focus on associative learning and memory of elementary adaptive; skilled movements, using classical conditioning of discrete movement (e.g., eyeblink, limb flexion). In this contract period we have developed extensive evidence for the following:</p> <p>1) using a tone conditioned stimulus (CS), the CS pathway involves the pontine nuclei and their mossy fiber projections to the cerebellum, 2) the unconditioned stimulus (US) reinforcing pathway involves the dorsal accessory olive and its climbing fiber projections to the cerebellum, 3) the CR pathway projects from the interpositus nucleus of the cerebellum to the red nucleus, 4) the memory trace appears to be formed in the cerebellum. Our computational/mathematical work involves a neural network model of the cerebellum and its associated brain stem circuitry, constrained by the biological properties of this neural system, and is increasingly successful in accounting for the properties of learning and memory of skilled movements.</p>					
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FINAL TECHNICAL REPORT  
OFFICE OF NAVAL RESEARCH CONTRACT #N0014-88-K-0112  
RICHARD F. THOMPSON, PRINCIPAL INVESTIGATOR  
NEUROSCIENCES PROGRAM  
UNIVERSITY OF SOUTHERN CALIFORNIA  
PERIOD: 2/1/88 - 1/31/91

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During this period we published a total of 24 papers supported by our ONR contract. The basic goal of our research is to localize and analyze processes and mechanisms of memory formation, storage and retrieval in the mammalian brain. We focus on associative learning and memory of elementary adaptive, skilled movements. Potential applications of our work range from enhancing memory and performance in humans to new principles of memory coding and storage in nonbiological systems to robotics. Our publications are in three broad categories: empirical neurobiological analyses of key brain systems, theoretical neurobiological and computational/mathematical modeling, and reviews of our work and the field. The 24 reprints are enclosed, listed in chronological order in the bibliography, and numbered for convenient reference. We present here a very brief overview of the work in each category.

Empirical Neurobiological Analysis

In earlier work (see 20 for review) we developed considerable evidence for a theoretical model of the brain circuitry essential for a basic form of association learning and memory: classical conditioning of discrete, skilled behavioral responses. In brief, this circuitry is the cerebellum and its associated brain stem circuits. In this contract period we developed considerable evidence that: 1) the CS pathway relays via the pontine nuclei and their mossy fiber projections to the cerebellum (1,6,9,13,17), 2) the critical US pathway includes the cells of origin of climbing fibers in the dorsal accessory olive (DAO) and normal learning occurs when the CS is stimulation of the pontine nuclei and the US is stimulation of the DAO climbing fibers (15). This (15) is a particularly important paper in that it implicates long-term-depression (LTD) as the synaptic mechanism of memory storage in

cerebellar cortex. Other studies focussed on the CR pathway from interpositus to behavior, the critical circuit being projections from interpositus to magnocellular red nucleus, and showed that the memory traces are not stored in the red nucleus (3,10,24). A study focussing on control procedures evaluated the role of the cerebellum in alpha conditioning (4). Perhaps the most striking result we have obtained to date is that this type of learning involves a clear structural change in the cerebellum, specifically a decrease in distal dendritic branching of Purkinje neurons in lobule H VI for trained animals compared to random stimulation control animals, implying decreased numbers of parallel fiber synapses (a structural correlate of LTD?) (20).

### Theoretical Modeling

As noted above, we have developed a theoretical neurobiological model of the neural circuitry essential (necessary and sufficient) for the learning and memory of discrete behavioral responses involving the cerebellum and its associated brain stem circuits (5,14,20). A major discovery in our combined neurobiological and modeling work concerns a possible neural circuit level instantiation of the basic LMS error correcting algorithm in adaptive filter networks and in the Rescorla-Wagner theory (16). In our computational/mathematical modeling we have developed an increasingly specific "top-down" approach, constrained by the actual connections and functional properties of the real neural network (18,21). In the most recent paper, we draw detailed parallels between neuronally constrained models of learning of adaptive movements and adaptation of the vestibulo-ocular reflex, utilizing the LMS spectrum analyzer model of response topography (22).

### Reviews

In review papers we have developed the evidence for our theoretical neurobiological model (2,7,8,11) and focussed on the nature of the essential reinforcement or teaching circuits in the brain for the learning of discrete, skilled movements (12,19).

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